Acupuncture as a complementary therapy in chemotherapy-induced nausea and vomiting

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The effect of acupuncture on chemotherapy-induced nausea and vomiting has been studied over the past 20 years, and clinical evidence gathered to date has been favorable. Current practice guidelines recommend acupuncture as a complementary therapy for uncontrolled nausea and vomiting induced by chemotherapy. Nevertheless, a placebo effect may have been present in studies that had no control group, and unanswered questions remain—particularly since newer and more effective antiemetic medications have become available. A research study employing adjunctive electroacupuncture for both acute and delayed chemotherapy-induced nausea and vomiting is proposed to address some of the unanswered questions.

Acupuncture is a therapeutic technique that involves inserting and manipulating thin needles into points on the body called acupuncture points. Acupuncture has been a very important part of traditional Chinese medicine. According to Chinese philosophy, *qi* (vital energy) is circulating within the human body. Diseases develop when *qi* is blocked. The pathways of running *qi* are called the meridians. Each meridian comprises an internal and an external pathway. The meridians' internal pathways connect to 12 internal organs, and their external pathways extend to the skin, which is where the acupuncture points lie. Acupuncture treats diseases by stimulating the acupuncture points and removing the blockage of *qi*. There are more than 400 acupuncture points on the human body located along 14 channels, which include 12 meridians and 2 extrameridians *(Figure 1)*. It needs to be pointed out that the acupuncture points and meridians have no anatomical or histological basis.

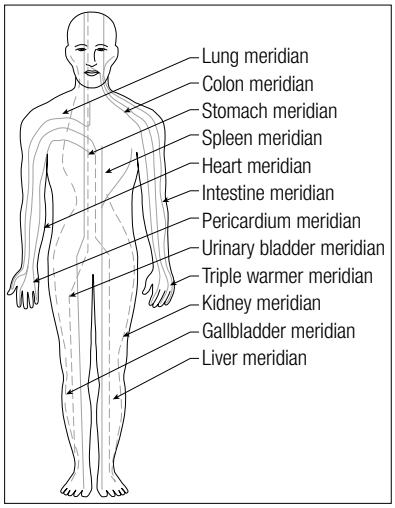

Figure 1. The 12 meridians of acupuncture.

Acupuncture dates back more than 4000 years. *Bian shi* (sharpened stones) were found in ruins in China dating back to the Stone Age; these stones are thought to be the earliest acupuncture needles. Metal acupuncture needles later were developed and replaced *bian shi*. Nowadays, the most popular acupuncture needles are sterilized disposable stainless steel needles, which are 0.18 to 0.51 mm in diameter *(Figure 2)*. The acupuncture needles are generally thinner than injection needles. Unlike injection needles, they are not hollow. Thus, acupuncture causes very minimal bleeding or pain.

Although acupuncture has been used to treat various diseases and conditions for thousands of years in China and in several other countries, it did not become popular in the United States until the last few decades. Acupuncture was first introduced to the United States by nontraditional Chinese medicine practitioners, mainly the early Chinese immigrants. In 1970s, American visitors to China brought back first-hand reports of patients receiving acupuncture for therapeutic purposes. Since then, many clinical studies have examined the effectiveness of acupuncture. Acupuncture is now recognized in the United States, where it is used to treat many conditions including headache, back pain, nausea, stress, infertility, fatigue, allergic sinusitis, neuralgia, and smoking cessation.

Although further studies are needed to investigate the mechanism of acupuncture, it is generally believed that acupuncture works mainly on the nervous system. Neuroimaging studies have demonstrated specific and predictable areas of brain activation/deactivation based on the function of a specific acupuncture point. Naloxone was found to block the analgesic effect of acupuncture, indicating that the release of natural endorphins in the brain is involved in the process (1, 2).

THE USE OF ACUPUNCTURE IN CONTROLLING CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Chemotherapy-induced nausea and vomiting is a common problem that can severely impair a patient's quality of life.

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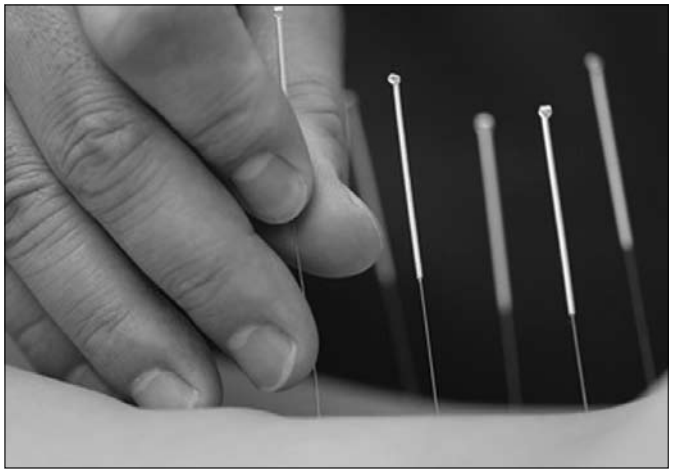

Figure 2. Thin, sterile needles used for acupuncture. Photo reprinted courtesy of Dreamstime.

Despite the availability of the newer antiemetic medications, many patients still suffer from these symptoms.

In the past 20 years, studies have been conducted of acupuncture's ability to control nausea and emesis following chemotherapy. All the studies have been carried out using acupuncture, electroacupuncture, acupressure, or electrostimulation wristbands as an adjunct to antiemetic pharmacotherapy. Electroacupuncture involves applying small electrical currents to the needles inserted at specific acupuncture points. It supplies consistent stimulation and is easier to practice than manual manipulation. Acupressure involves a physical pressure applied to the acupuncture points by hand, elbow, or various devices. It is noninvasive but is thought to be less effective than manual acupuncture or electroacupuncture. Electrostimulation wristbands supply continuous electrical stimulation to the acupuncture points.

The acupuncture points that have been widely used for nausea control are P6 and ST36. P6 *(neiguan)* is located between the tendons of palmaris longus and flexor carpi radialis at 2-body-inches proximal to the wrist crease (1 body-inch is the greatest width of a patient's thumb at the distal phalanx). ST36 *(zusanli)* is on the anterior lateral side of the leg, 1 body-inch from the anterior crest of the tibia.

Based on the published studies, two practice guidelines were developed that supported the use of acupuncture for chemotherapy-related nausea and vomiting (3, 4). The American College of Chest Physicians addressed the use of acupuncture as follows:

> Acupuncture is recommended as a complementary therapy when nausea and vomiting associated with chemotherapy are poorly controlled. Grade of recommendation, 1b.
>
> Electrostimulation wristbands are not recommended for managing chemotherapy-induced nausea and vomiting. Grade of recommendation, 1b (4).

The 1997 National Institutes of Health Consensus Statement indicated that "promising results have emerged . . . showing efficacy of acupuncture in adult postoperative and chemotherapy nausea and vomiting" (5). This statement was based on 33 controlled trials, of which 27 showed positive results in favor of acupuncture, electroacupuncture, or acupressure at acupuncture point P6. Among those trials were two randomized controlled trials in postchemotherapy patients (6, 7). Both of the studies showed favorable results for electroacupuncture.

Since then, more trials have been carried out to investigate the effect of acupuncture on postchemotherapy nausea and vomiting. Randomized controlled, parallel, and crossover studies demonstrated the benefit of electroacupuncture in acute chemotherapy-induced vomiting (within 24 hours after chemotherapy). However, none of these trials were done in conjunction with modern antiemetics, such as the 5-hydroxytryptamine-3 (5-HT_3) receptor antagonists (ondansetron, granisetron, dolasetron, and palonosetron) approved by the US Food and Drug Administration between 1991 and 2003. In addition, acupuncture has not been proven to relieve the delayed nausea that occurs from 1 to 8 days after chemotherapy (8–13).

Since the 5-HT_3 receptor antagonists have become available, most studies have focused on electric stimulation or acupressure, which might not be as effective as the invasive manual or electroacupuncture. Most trials on acupressure did not show significant protective effects on the control of acute nausea and vomiting or delayed symptoms (14, 15). Only a few studies (16–18) suggested the antiemetic effects of acupressure in postchemotherapy patients.

A recent study (17) recruited 100 patients with metastatic solid tumors; these patients had received chemotherapy and had no response to 5-HT_3 receptor antagonists, corticosteroids, and antidopaminergic agents. The P6 acupoint was stimulated by acupressure with a button for 8 hours a day starting before chemotherapy and continuing for at least 3 days after chemotherapy. In this study, 68% of the patients achieved control of emesis, not dependent on tumor histotype. However, this study was not a randomized controlled trial and did not indicate the difference between early and delayed antiemetic efficacy.

A multicenter randomized controlled trial of 160 women receiving chemotherapy for breast cancer (18) found no effect of acupressure on acute nausea and vomiting but found reduction of delayed nausea and vomiting by acupressure. Electrostimulation wristbands, which supply continuous electrical stimulation to the antiemetic acupuncture point, have been shown to have no benefit in controlling nausea and vomiting. Moreover, these wristbands could act as a conditioned stimulus of nausea and thus worsen the nausea in some patients (3, 4).

To date, only one study has evaluated manual acupuncture in conjunction with modern antiemetics (19). That study showed no effect of acupuncture beyond the effect of intravenous ondansetron. Ezzo et al (15) suggested two explanations. One was that acupuncture might not offer anything beyond what modern antiemetic regimens can offer due to a shared pathway of action. Another explanation was that the statistical power of the study (80%) might not be large enough to demonstrate a meaningful effect.

These studies are summarized in the *Table.*

The biggest problem with acupuncture studies has been placebo effect. Only several of the previous studies (6, 8, 18,

Table. Summary of some recent studies on the effectiveness of acupuncture

First author, year (ref)	Randomized trial	Use of 5-HT_3 antagonists	Use of sham control	Favorable result to acupuncture	Study of acute or delayed emesis	Type of procedure
Dundee, 1987 (6)	Yes	No	Yes	Yes	Only acute studied	Electroacupuncture
Dundee, 1989 (7)	Yes	No	No	Yes	No differentiation	Electroacupuncture
Shen, 2000 (8)	Yes	No	Yes	Yes	No differentiation	Electroacupuncture
Aglietti, 1990 (10)	No	No	No	Yes	Only acute studied	Manual acupuncture
Dundee, 1990 (11)	No	No	No	Yes	Only acute studied	Acupressure
Dundee, 1991 (13)	Yes	No	No	Yes	No differentiation	Transcutaneous electrical stimulation
Roscoe, 2003 (14)	Yes	Yes	No	Yes	Reduction of acute, no effect on delayed	Acupressure
McMillan, 1991 (16)	Yes	Yes	No	Yes	No differentiation	Transcutaneous electrical stimulation
Gardani, 2007 (17)	No	Yes	No	Yes	No differentiation	Acupressure
Dibble, 2007 (18)	Yes	Yes	Yes	Yes	No effect on acute, reduction of delayed	Acupressure
Streitberger, 2003 (19)	Yes	Yes	Yes	No	Only acute studied	Manual acupuncture

19) used sham control (blunted needle intervention at the antiemetic acupuncture point, or acupuncture or acupressure at acupuncture points believed to be unrelated to nausea control) to avoid the placebo effect of acupuncture or acupressure. In the remainder of the studies, control groups were not used. Shen et al (8) applied minimal needling at two acupuncture points that are believed to be unrelated to nausea control in the control group. Although their study showed favorable results for electroacupuncture, it did not include the 5-HT_3 receptor antagonists. Streitberger et al (19) applied manual acupuncture to the study group, while the control group received electrostimulation with a blunted placebo needle to simulate an acupuncture procedure without penetrating the skin. Their study showed no additional effect in combination with intravenous ondansetron on the prevention of nausea and vomiting in high-dose chemotherapy. Dibble et al (18) used acupressure on a sham point as control and demonstrated that acupressure reduced the delayed but not the acute nausea and vomiting.

SAFETY AND COST OF ACUPUNCTURE

The adverse events documented for acupuncture have been very minimal (15, 20–22). Ezzo et al (15) pooled 11 trials (N= 1247). Only one patient felt electrical shock, and one patient with peripheral neuropathy had aggravation of tingling. Summarizing nine surveys, Ernst et al (20) found that the most common adverse events were needle pain (1%–45%), bleeding (0.03%–38%), and faintness or syncope (0%–0.3%). The potential risks are generally thought to include bruising, bleeding, hematoma, pain, infection, possible fainting, aggravation of neuropathy, and feeling of electrical shock. Safety precautions that need to be taken include using thin needles to minimize pain or bleeding, using sterile needles to minimize risks of infection, using weak and safe electrical current in electroacupuncture to avoid electrical shock, and ensuring that acupuncturists have good knowledge of local anatomy to avoid nerve or other damage.

What about the cost of acupuncture? Fees for a typical acupuncture visit range from $75 to $100 depending on the practitioner. Acupuncture is thought to be a very cost-effective therapy for nausea control in patients receiving chemotherapy compared with hospitalization and expensive intravenous medications for the intractable nausea, dehydration, and electrolyte abnormalities these patients might experience. However, formal studies need to be carried out to assess the cost-effectiveness of acupuncture in addition to the pharmacological antiemetic regimens in these patients.

PROPOSED STUDY

Based on a review of published data on acupuncture, several questions remain. Two of the main questions are as follows:

1. What is the efficacy of acupuncture in controlling delayed chemotherapy-induced emesis (2–5 days after chemotherapy)?
2. Does acupuncture offer antiemetic effects in addition to those of modern antiemetic regimens (5-HT_3 receptor antagonists)?

A study is proposed to investigate the effect of acupuncture on the control of chemotherapy-induced nausea and vomiting

that is not controlled completely with modern pharmacological regimens.

Although both manual acupuncture and electroacupuncture are believed to be more effective than noninvasive electrostimulation or acupressure, manual acupuncture requires more skilled technique, and the consistency of efficacy is difficult to control among different acupuncturists. The proposed study would use electroacupuncture at point P6. This technique is easier to perform and provides better consistency than manual acupuncture and yet is believed to be more effective than noninvasive electrostimulation or acupressure. Electroacupuncture would be used in conjunction with modern antiemetic medications.

A statistical power of 90% is proposed, which is higher than that of the only study involving acupuncture in conjunction with modern antiemetics (19). Both early and delayed post-chemotherapy nausea and vomiting would be studied.

A sham control would be obtained by electroacupuncture at acupuncture point LU7 *(lieque),* which is located on the lateral aspect of the radius proximal to the styloid process. Acupuncture at LU7 is commonly used to treat headaches, cough, and sore throat but is not known to be effective in controlling nausea.

The study could provide evidence of the effect of acupuncture on the control of chemotherapy-induced nausea and vomiting when used in conjunction with newer antiemetic medications. If proved to be effective, acupuncture could provide a safe and easy way to improve the quality of life of cancer patients who receive chemotherapy. Funding for this study is currently being sought.

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